[3.2]Metacyclophanes. Transannular Cyclization and Ring Expansion

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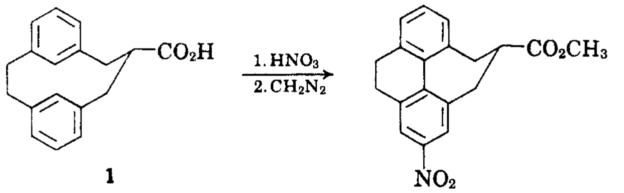
Nitration of [3.2]metacyclophane-2-carboxylic acid proceeds slowly under mild conditions to give a product of a transannular cyclization, 2-nitro-4,5-(2′-carboxypropano)-9,10-dihydrophenanthrene. Dimethyl-2-[3.2]metacyclophanylmethanol was transformed *via* its acetate ester to a mixture of olefins which yielded 2,3-dimethyl[4.2]metacyclophan-1-ene when subjected to acid catalysis.

The ability of [2.2]metacyclophane to undergo transannular cyclization during dehydrogenation,[2] bromination,[3] and nitration[4] has been reported. This cyclization has been found to be reversible in the case of 8,16-dialkyl[2.2]metacyclophane-1,9-diene.[5] In the case of nitration, Allinger[4] has explained this cyclization upon electrophilic substitution by a mechanism involving the simultaneous attack by the developing phenonium ion on the opposing benzenoid ring. It was of interest to determine if this unusual reaction extended to the [3.2]metacyclophane system where the distance between aromatic rings is increased by *ca.* 25%.[6]



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It was found that nitration of [3.2]metacyclophane-2-carboxylic acid[7] proceeds slowly under mild conditions (4 *N* nitric acid in acetic acid). If the reaction is allowed to proceed for a period of 72 hr at room temperature, a 30–35% yield of one product can be isolated following methyl esterification of the crude product mixture. This product was assigned the structure 2-nitro-4,5-(2′-carbomethoxypropano)-9,10-dihydrophenanthrene (2) on the basis of spectral evidence.

The infrared spectrum of the product showed strong absorption indicative of the ester carbonyl (5.79 μ) and the nitro group (6.63 and 7.46 μ). In the ultraviolet absorption spectrum, the longest wavelength absorption maximum at 334 mμ (log ϵ 4.11) represents an 18-mμ hypsochromic shift from the corresponding maximum at 352 mμ (log ϵ 4.24) observed in 2-nitro-4,5,9,10-tetrahydropyrene.[8] This shift is comparable with the 16-mμ hypsochromic shift observed between the longest wavelength absorption maxima in the ultraviolet spectra of 9,10-dihydrophenanthrene and 2,2′-trimethylenebiphenyl.[9] An increase in the dihedral angle between ring planes produces this shift and decrease in extinction. The ultraviolet spectrum and the absence of a high-field aromatic proton resonance signal which is characteristic of the lower members of the [*m.n*]metacyclophanes[10,11] provides good evidence that a transannular cyclization has occurred.

The aromatic proton magnetic resonance consisted of two sharp signals at δ 7.17 and 8.00 ppm, integrating in the ratio 3:2. This is consistent with substitution *meta* to the methylene bridges. Introduction of a nitro group in positions *ortho* to the bridges would be expected to give rise to two proton signals from that ring separated by *ca.* 30 Hz in addition to that arising from the other ring.[12] The methylene proton resonance signals at 2.77 and 2.83 ppm are sharp at room temperature but broaden noticeably below −25°. This is inconsistent with the energy barriers to ring inversion in [3.2]metacyclophanes[7] but reasonable for the cyclized structure 2 based on the estimation of barriers in 3,5-dibenzoxepine and analogous systems.[13]

The other components of the crude reaction mixture were the ester of the starting material (30% recovery) and an orange-colored oil which was more strongly absorbed on alumina during chromatography than either of the two identified components. Thin layer chromatography showed this oil to be composed of at least three colored compounds. Insufficient data were obtained to permit structural assignments for these compounds. The above results do not rule out the possibility of nitration yielding a mononitro derivative without transannular cyclization, but the expected properties of such a derivative should have allowed its detection.

The results of the nitration experiment appear consistent with the previously proposed mechanism.[4] The diminished rate of the reaction can be explained by the lower strain energy in the [3.2]metacyclophane system and the increased separation between aromatic rings produced by the three-membered bridge. However, preliminary studies of the nitration of 5,13-dimethyl[2.2]metacyclophane indicate that transannular cyclization occurs readily even when the substituent

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(2) W. Baker, J. F. W. McOmie, and J. M. Norman, *J. Chem. Soc.*, 1114 (1951).

(3) V. Boekelheide, W. S. Lindsay, and R. W. Griffin, Jr., unpublished results cited by W. S. Lindsay, P. Stokes, L. G. Humber, and V. Boekelheide, *J. Am. Chem. Soc.*, **83**, 943 (1961).

(4) N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *ibid.*, **83**, 1974 (1961).

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(6) The distance between C_9 and C_{17} was approximated with a model incorporating some of the strain evident in [2.2]metacyclophane; see C. J. Brown, *J. Chem. Soc.*, 3278 (1953).

(7) R. W. Griffin, Jr., and R. A. Coburn, *J. Am. Chem. Soc.*, **89**, 4638 (1967).

(8) The ultraviolet spectrum of this compound was obtained from a sample prepared from [2.2]metacyclophane according to the procedure of Allinger.[4]

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(10) R. W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963).

(11) R. W. Griffin, Jr., and R. A. Coburn, *Tetrahedron Letters*, **37**, 2571 (1964).

(12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 259.

(13) R. J. Kurland, M. B. Rubin, and W. B. Wise, *J. Chem. Phys.*, **40**, 2426 (1964).

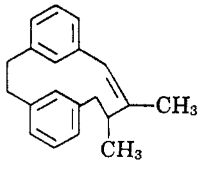
enters *ortho* to the bridges.[14] Alkylbenzenes have recently been reported to undergo oxidative coupling with nitric acid to form unnitrated biphenyls.[15] Such an initial step in the case of [*m.n*]metacyclophanes would explain the substitution pattern but not the unusual rate of reaction. Clearly, a more careful investigation including kinetic studies is warranted to confirm the proposed mechanism.

Ring Expansion.—In continuation of the study of the [*m.n*]metacyclophanes, ring expansion of a [3.2]-metacyclophane appeared to be a potential synthetic route to [4.2]metacyclophanes. Interest was centered upon the extent to which the physical and chemical interactions between benzenoid rings in [2.2]- and [3.2]-metacyclophanes are reflected in the larger ring homologs.

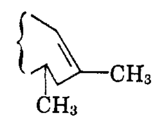
It was anticipated that, if a carbonium ion could be generated with the electron-deficient carbon atom α to the 11-membered ring, the nonbonded strain in the [3.2]metacyclophane system would provide a driving force for the ring expansion. Pyrolysis of the acetate ester of dimethyl-2-[3.2]metacyclophanylmethanol produces an oil whose infrared and nmr spectral properties can best be accounted for by a composition of *ca.* 25% 2-isopropylidene[3.2]metacyclophane and 75% 2-isopropenyl[3.2]metacyclophane.[16] Owing to the difficulty experienced in attempts to separate the components of this mixture by elution column chromatography or vpc, the entire mixture was subjected to acid catalysis. A single crystalline product, isolated in 43% yield, was obtained from this treatment. This product was assigned the structure 2,3-dimethyl[4.2]-metacyclophane-1-ene on the basis of infrared, nmr, and mass spectral evidence.

The nmr spectrum showed the following signals: a six-proton multiplet at δ 6.5–7.2 ppm (aromatic), three one-proton singlets at 4.62, 5.62, and 6.06 (10-,18- and vinyl), a seven-proton multiplet at 2.0–3.5 (protons on saturated carbon in the bridges), a three-proton doublet at 1.63 (methyl group on unsaturated carbon, $J = 1$ Hz), and a three-proton doublet at 0.97 (methyl group on saturated carbon, $J = 6$ Hz). The [4.2]-metacyclophane structure was suggested by the high-field aromatic proton signals while the [3.2]metacyclophane structure was discredited by the sharp bridging methylene proton signals which remained invariant over the temperature range -50 to 70°. This indicates that rapid ring inversion is occurring in this temperature range, which would be anomalous for the [3.2]metacyclophane system.[7]

The presence of two different methyl groups indicates that the rearrangement was more extensive than a simple ring expansion. The structures A–F are compatible with the general features of the nmr spectrum.



A



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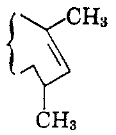
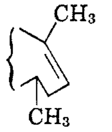
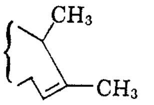


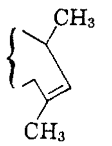
C



D



E

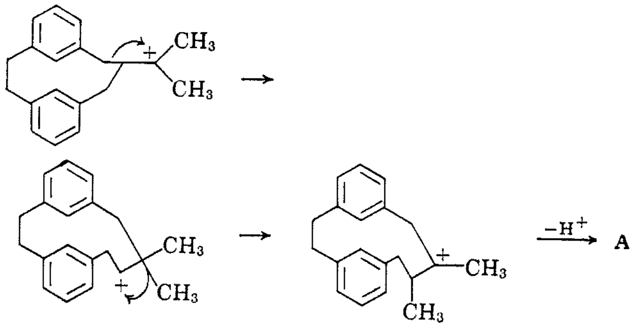


F

The singlet, olefinic proton resonance signal supports structures A and B over the others in which the signal would be expected to be a doublet or multiplet. The mass spectral fragmentation pattern of this compound furnishes evidence that the double bond is in the 1 position and that a methyl group is not in the 4 position (structures A and C). A very intense peak (100%) at *m/e* 157 was found in the fragmentation pattern,[17] which corresponds to a $C_{12}H_{13}^+$ ion arising in a direct process from the prominent (20%) parent molecular ion at *m/e* 262. This is indicated by the metastable ion peak at *ca. m/e* 94. Such a process would not be so highly favored in olefins E and F as it would be in structures A–D.

The formation of the final product, following ring expansion, results from methyl migration to give a tertiary carbonium ion as shown in Scheme I.

SCHEME I



The ultraviolet absorption spectrum of 2,3-dimethyl[4.2]metacyclophane-1-ene exhibited maxima characteristic of the 1,3-dialkylbenzene group, $\lambda_{\max}^{\mathrm{EtOH}}$ 208 mμ (log ϵ 4.75) and 265.5 mμ (log ϵ 2.62), but affording no indication of a conjugated double bond. Examination of Dreiding models shows that in the preferred conformations the double bond is nearly orthogonal to the aromatic ring. The 260-mμ absorption band shows a negligible bathochromatic shift compared with that observed in [2.2]- and [3.2]metacyclophanes.

The 2-mono- and 2,2-disubstituted[3.2]metacyclophanes[7] exhibited a maximum at 269 ± 0.5 mμ. This corresponds to a bathochromatic shift of 4 mμ relative to the open chain model, 1,2-bis(3-methylphenyl)-ethane. The extent to which this shift represents a transannular electronic effect or merely the deformation of the aromatic rings is not clear. In the case of [2.2]metacyclophane, the observed shift of the 260-mμ band is larger but the effect is still small in comparison with the accuracy of the calculation of the results expected from transannular resonance.[4]

These investigations demonstrate the practicality of synthesizing the [4.2]metacyclophane structure from [3.2]metacyclophane precursors and provide an insight

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(14) R. W. Griffin, Jr., and G. Detre, unpublished results.

(15) I. Puskas and E. K. Fields, paper presented at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla, April 1967.

(16) This less direct method was chosen in hope of obtaining sufficient 2-isopropylidene[3.2]metacyclophane to allow the preparation of [3.2]metacyclophan-2-one.

(17) Mass spectra were recorded with an AEI MS-9 high-resolution mass spectrometer using a direct sample insertion technique with a source temperature of 120° (70 ev).

into the extent to which the interesting properties of the [2.2]metacyclophanes are reflected in their larger homologs.

Experimental Section

Melting points were determined with a Fisher-Johns melting point apparatus and are corrected. Ultraviolet spectra were recorded with a Cary spectrophotometer, Model 11M. Infrared spectra were obtained with a Perkin-Elmer grating spectrophotometer, Model 237. Nmr spectra were recorded with a Varian A-60 nmr spectrometer.

Nitration of [3.2]Metacyclophane-2-carboxylic Acid (1).—A solution of [3.2]metacyclophane-2-carboxylic acid (100 mg, 0.375 mmole), glacial acetic acid (30 ml), and 70% nitric acid (10 ml) was maintained at 30–35° for 72 hr. The solution was poured on to crushed ice (100 g) and stirred. Water (100 ml) was added and the solution was extracted with five 20-ml portions of ether. The combined ether extract was washed with distilled water and with saturated salt solution, and then dried over anhydrous magnesium sulfate. Evaporation of the ether gave 104 mg of orange oil to which an ethereal solution of diazomethane (0.4 mmole) was added. The solvent was evaporated and the resulting oil taken up in carbon tetrachloride (0.25 ml) and placed on a column of 3 g of alumina (Woelm, neutral, activity grade I). Elution with benzene gave an early fraction containing 35 mg of colorless oil identified as methyl [3.2]metacyclophane-2-carboxylate by comparison of its nmr and infrared spectra with those of an authentic sample.[7]

A latter fraction, eluted with benzene, contained 37 mg (31% yield) of 2-nitro-4,5-(2′-carbomethoxypropano)-9,10-dihydrophenanthrene as a pale yellow oil. Repeated recrystallization from methanol gave 15 mg of yellow plates, mp 134–136°. The composition was determined by a high resolution mass spectrometric measurement. An exact mass measurement of the C^{13}-containing molecular ion was found to be *m/e* 324.1193. This agrees well with the molecular ion $C_{19}H_{17}NO_4^+$ containing one atom of C^{13} calculated[18] to exhibit *m/e* 324.1190.

A final fraction eluted from the column with ether contained 20 mg of orange oil. Thin layer chromatography (Woelm alumina plate developed in methylene chloride) of this material gave one red and two yellow spots, demonstrating the presence of at least three colored products. None of the components was isolated in sufficient quantity for identification.

2,3-Dimethyl[4.2]metacyclophan-1-ene.—A solution of dimethyl-2-[3.2]metacyclophanylmethanol[7] (200 mg, 0.714 mmole), glacial acetic acid (3 ml), and acetic anhydride (1 ml) was refluxed for 6 hr. The solvent was removed under reduced pressure and the residue taken up in ether (5 ml). This ether solution was washed with distilled water, 10% sodium bicarbonate solution, and saturated salt solution, dried over anhydrous magnesium sulfate, and evaporated. The infrared spectrum of the resulting oil exhibited no absorption at 2.83 and 5.79 μ (indicative of starting alcohol and its acetate ester) which had been observed when shorter reaction periods were employed. Although the oil showed two spots on thin layer chromatography (Woelm alumina plate developed in petroleum ether (bp 30–60°)), elution column chromatography on a column of 3 g of alumina (Woelm, neutral, activity grade I) failed to give a separation. Vapor phase chromatography using an Apiezon L column likewise gave only a broad unresolved band.

The nmr spectrum of the product taken in carbon tetrachloride contains a singlet at 5.35 ppm assigned to the 9,17 protons of 2-isopropylidene[3.2]metacyclophane, while a more complex multiplet at 4.8 ppm is assigned to the terminal olefinic and 9,17 protons of 2-isopropenyl[3.2]metacyclophane. Integration of these signals indicates a composition of *ca.* 1:3, respectively. This composition is supported by integration of the methyl protons signal (1.76 ppm) which indicates 3.8 protons (25% of six protons plus 75% of three protons). Strong absorption at 6.10 and 11.3 μ in the infrared taken as a neat liquid is indicative of a terminal olefin.

A solution of the olefinic mixture (169 mg), *p*-toluenesulfonic acid (50 mg), and glacial acetic acid (5 ml) was refluxed for 12 hr. The solvent was removed under reduced pressure and the residue taken up in ether (5 ml). The ether solution was washed with 10% sodium bicarbonate solution, distilled water, and saturated salt solution and dried over anhydrous magnesium sulfate. Evaporation of the ether gave 160 mg of semisolid residue which was taken up in petroleum ether and chromatographed on 2.5 g of alumina (Woelm). Elution with petroleum ether gave 73 mg (43% yield) of 2,3-dimethyl[4.2]metacyclophan-1-ene as white crystals, mp 101–102.5°.

Anal. Calcd for $C_{20}H_{22}$: C, 91.54; H, 8.46. Found: C, 91.63; H, 8.57.

Absorption at 11.9 μ (observable in chloroform solution) can be assigned to a vinyl hydrogen out-of-plane deformation. The ultraviolet absorption spectrum contains a broad maximum at 208 mμ (log ε 4.75) with a sharp shoulder at 265.5 mμ (log ε 2.62).

Registry No.—2, 14698-41-0; 2-isopropylidene[3.2]metacyclophane, 14633-62-6; 2-isopropenyl[3.2]metacyclophane, 14633-63-7; 2,3-dimethyl[4.2]metacyclophan-1-ene, 14698-42-1.

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[18] J. H. Beynon and A. E. Williams, "Mass and Abundance Tables for Use in Mass Spectrometry," American Elsevier Publishing Co., Inc., New York, N. Y., 1963.

The Reactions of *exo*- and *endo*-5-Chloromethylnorbornene with Sodium[1]

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The reaction of either *exo*- or *endo*-5-chloromethylnorbornene with sodium in *n*-decane generates 3- and 4-allycyclopentene, *cis*-bicyclo[3.3.0]octene-2, and bicyclo[3.2.1]octene-2. Mechanistic routes for these ring-cleavage and ring-cleavage rearrangement reactions are proposed.

While norbornyl and norbornenyl systems are known to undergo a variety of carbonium ion rearrangements, as a result of the intensive study which these rearrangements have provoked over approximately a twenty-year period,[3] very few investigations, by comparison, have focused attention on other intermediates in these ring systems. Recently we have reported[4] that the reaction of either nortricyclyl or dehydronorbornyl chloride with sodium in *n*-decane results in rearrangement and ring cleavage, yielding a nearly identical mixture of hydrocarbon products: nortricyclene, norbornene, and 3- and 4-vinylcyclopentene (eq 1). The possibility that a similar mechanistic pathway might be uncovered for the reactions of *endo*

[1] Abstracts, Northwest Regional Meeting of the American Chemical Society, Bellingham, Wash., June 1960, p 25.

[2] National Defense Education Act Fellow, 1959–1962.

[3] J. A. Berson, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, part I., Chapter 2; G. D. Sargent, *Quart. Rev.* (London), **20**, 301 (1966); G. E. Gream, *Rev. Pure Appl. Chem.*, **16**, 25 (1966); H. C. Brown, *Chem. Brit.*, **2**, 199 (1966).

[4] P. K. Freeman, D. E. George, and V. N. Mallikarjuna Rao, *J. Org. Chem.*, **28**, 3234 (1963); **29**, 1682 (1964).